

Pursuant to MPEP 210.06(d), section "PRIOR ELECTION," Applicants hereby expressly indicate that a shift in species election in the present application is desired.

Applicants have also amended claims 1, 3, 5-29 and 76 to correct obvious typographical errors. Applicants submit that there is no narrowing of scope in any respect due to these amendments.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants note that the amendments to claims 1, 3, and 23-25 will be entered for purposes of Appeal according to the Advisory Action (Paper No. 17) mailed on April 8, 2002.

Claim rejections under 35 U.S.C. 102(b)

The Office Action maintains that claims 1-5, 12-14, 20, and 23-28 are rejected under 35 U.S.C. 102(b), as being anticipated by Rueger et al., WO 94/03200. Specifically, the Office Action maintains that Rueger et al. teach animal models with intentionally induced lesions for purposes of evaluation and teach systemic administration, thus anticipating the limitations of the instant claims.

Accordingly, Applicants have amended claims 1, 3, and 5 to clarify that the claimed methods are for non-neuronal tissues, thus obviating the rejection.

Applicants submit that Rueger et al. disclose treatment methods, compositions and devices for maintaining neural pathways in a mammal (see, for example, the abstract and the 1st paragraph of page 1 of Rueger et al.). However, Rueger et al. do not teach or suggest any systemic administration of morphogens in any non-neuronal tissues, thus Rueger et al. fail to meet each and every aspect of the claimed inventions. In contrast, the instant application discloses in detail as to how the claimed invention can be practiced in various tissues, including (but are not limited to) skeletal, lung, cardiac, liver, pancreas, uterine, intestinal, gastrointestinal (GI) tract, orthopedic, chondrogenic, or thyroid tissue (page 3, pages 16-20, and Examples 1-8 (bone), 9 (lung), 10 (cardiac tissue), 11-12 (liver), 13 (oral mucosa), 14 (gastrointestinal tissue), 15 (renal), 16 (osteochondrial or chondral tissue)).

Therefore, all amended claims are novel over Rueger et al., and Rueger et al. do not anticipate the claimed invention. Thus, in view of the amendment and argument presented above, reconsideration and withdrawal of the rejection is respectfully requested.

Claim rejections under 35 U.S.C. 103(a)

The Office Action maintains that claims 8-11, 15-19, 21, and 22 are rejected under 35 U.S.C. 103(a), as being obvious in view of Rueger et al. (WO 94/03200) over Benet. Specifically, the Office Action maintains that although Rueger et al. do not teach basic features of the claims, in particular the site of administration and the method of creating the defect, evaluation of potential therapeutics in compromised animals is art standard, as disclosed by Benet, and is thus an obvious modification of the methods taught by Rueger et al.

In view of the amendment to claims 1, 3, and 5 as presented above, Applicants submit that none of the cited references teach or suggest systemic administration of morphogens to any animals, for purpose of evaluating the morphogenic activity / optimal dosage of a candidate morphogenic protein or analog in any non-neuronal tissues. In contrast, it is the instant application that first teaches that different morphogenic proteins / analogs might have different specific morphogenic activity and/or optimal dosage in any given organ / tissue (see page 3, 1st paragraph). Thus, even for the sake of argument, the combined teachings of Rueger et al. and Benet still do not teach or suggest all the limitations, especially the non-neuronal tissue aspect of the claimed invention.

In addition, even if what is alleged by the Office Action were true, none of the cited references offer any motivation for a skilled artisan to test morphogenic activity / optimal dosage in non-neuronal tissues.

And lastly, as none of the cited references discuss non-neuronal tissues, one of ordinary skill in the art would not have a reasonable expectation that the methods disclosed in the cited art would be effective in other unrelated tissue types.

Similar arguments also apply to Wang et al. There is no teaching or suggestion in Wang et al. that activity / optimal dosage of *systemically* administered morphogens can be evaluated in non-neuronal tissues. In fact, Wang et al. exclusively focus on administering morphogens to neuronal

tissues. In addition, Wang et al. do not even explicitly disclose that morphogens can be administered *systemically*.

Pursuant to MPEP 2143, “[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).”

Thus, based on the amendments and arguments presented above, none of the three basic requirements of a *prima facie* case of obviousness is met. Applicants submit that all claims as amended are non-obvious in view of the cited references. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. 103(a) is respectfully requested.

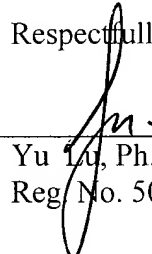
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims as amended are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Respectfully Submitted,



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